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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/715,017	11/17/2003	Arun Majumdar	028726-022	3299

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EXAMINER

LUM, LEON YUN BON

ART UNIT PAPER NUMBER

1641

DATE MAILED: 07/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/715,017

Applicant(s)

MAJUMDAR ET AL.

Examiner

Leon Y. Lum

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 25 January 2005.  
2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-82 is/are pending in the application.  
4a) Of the above claim(s) 1-63 is/are withdrawn from consideration.  
5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
6) ☒ Claim(s) 64-82 is/are rejected.  
7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.  
10) ☒ The drawing(s) filed on 17 November 2003 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)  
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 10/12/04, 11/15/04, 1/25/05  
4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_  
5) ☐ Notice of Informal Patent Application (PTO-152)  
6) ☐ Other: \_\_\_\_\_

5,000

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
  - I. Claims 1-22 and 62, drawn to a system for detecting target molecules, classified in class 422, subclass 57.
  - II. Claims 23-38, drawn to a method, classified in class 435, subclass 7.1.
  - III. Claims 39-40, drawn to a method, classified in class 435, subclass 287.9.
  - IV. Claims 41-58 and 63, drawn to a system, classified in class 422, subclass 83.
  - V. Claims 59-61, drawn to a microcantilever, classified in class 422, subclass 99.
  - VI. Claims 64-82, drawn to a system for detecting target molecules, classified in class 422, subclass 68.1.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions I and II are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP §

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806.05(e)). In this case the apparatus as claimed can be used in the materially different process of liquid filtration, wherein a flow of liquid sample is applied over the surface of the sensors and the probe molecules bind to associated target molecules, thereby removing the target molecules from the flow of liquid sample and filtering the liquid sample.

This relationship also applies to Groups I and III.

3. Inventions I and IV-VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation and different functions.

Group I is a system with the limitations of an optical detector and wherein the property of the reflected beam of light is an intensity of at least a portion of an interference pattern, which are not limitations in Groups IV-VI.

Group IV is a system with the limitations of a sensor base portion, plurality of access channels, wherein each of the plurality of access channels is associated with one of the plurality of regions, and wherein the plurality of access channels share a common outlet, which are not limitations in Groups I and V-VI.

Group V is a microcantilever with the limitation of a microcantilever body, which is not a limitation in Groups I, IV, and VI.

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Group VI is a system with the limitations of an array of microsenors, an optical detector array configured to simultaneously detect the position of each of the microsenors, and wherein the optical beam is a collimated beam of laser light, which are not limitations in Groups I and IV-V.

Therefore, Groups I and III-V have different modes of operation and different functions that distinguish them as unrelated inventions.

4. Inventions II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects. (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation and different functions. Group II is a method with the limitation wherein each of the plurality of sensors is functionalized to detect a different target material, which is not a limitation in Group III. Group III is a method with the limitation wherein each of the plurality of sensors is functionalized to detect the same target material, which is not a limitation in Group II.

Therefore, Groups II-III have different modes of operation and different functions that distinguish them as unrelated inventions.

5. Inventions II and IV are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another materially different apparatus or by hand, or (2) the apparatus as

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claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case the apparatus as claimed can be used in the materially different process of liquid filtration, wherein a flow of liquid sample is applied over the surface of the sensors and the probe molecules bind to associated target molecules, thereby removing the target molecules from the flow of liquid sample and filtering the liquid sample.

This relationship also applies to Groups II and V-VI.

6. Inventions III and IV are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case the apparatus as claimed can be used in the materially different process of liquid filtration, wherein a flow of liquid sample is applied over the surface of the sensors and the probe molecules bind to associated target molecules, thereby removing the target molecules from the flow of liquid sample and filtering the liquid sample.

This relationship also applies to Groups III and V-VI.

7. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

In addition, because these inventions are distinct for the reasons given above and the search required for each of Groups I-VI is not required for the other Groups, restriction for examination purposes as indicated is proper.

Group I is a system which requires searching for an optical detector and wherein the property of the reflected beam of light is an intensity of at least a portion of an interference pattern, which are not required searches for Groups II-VI.

Group II is a method with required searching for the limitations wherein each of the plurality of sensors is functionalized to detect a different target material, rejecting individual pixel values, and applying a gain factor algorithm, which are not required searches for Groups I and III-VI.

Group III is a method with required searching for the limitation wherein each of the plurality of sensors is functionalized to detect the same target material, which is not a required search for Groups I-II and IV-VI.

Group IV is a system with the limitations of a sensor base portion, plurality of access channels, wherein each of the plurality of access channels is associated with one of the plurality of regions, and wherein the plurality of access channels share a common outlet, which are not limitations in Groups I-III and V-VI.

Group V is a microcantilever with the limitation of a microcantilever body, which is not a limitation in Groups I-IV, and VI.

Group VI is a system with the limitations of an array of microsensors, an optical detector array configured to simultaneously detect the position of each of the

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microsensors, and wherein the optical beam is a collimated beam of laser light, which are not limitations in Groups I-V.

8. During a telephone conversation with David Heckadon on 22 March 2005 a provisional election was made without traverse to prosecute the invention of Group VI, claims 64-82. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-63 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

9. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

### ***Drawings***

10. Figures 2A-B should be designated by a legend such as --Prior Art-- because only that which is old is illustrated. See MPEP § 608.02(g). Corrected drawings in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct



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any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

The instant figures are depicted in Wu et al (PNAS, 2001), which is cited in the IDS filed 12 October 2004. In addition, any other figures in the drawings that have been published in the prior art must also be designated by the same legend.

### ***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claim 69 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claim recites the term "stiffened portion" in line 2. However, the specification does not include this term and the drawings do not indicate any portion of the microsensors that would comprise this limitation. Since the instant claim is classified as "New" and was not submitted on the same date as the filing date of the application, the instant term is considered to be new matter.

***Claim Rejections - 35 USC § 102***

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 64-73, 77-80, and 82 are rejected under 35 U.S.C. 102(b) as being anticipated by Fritz et al. (Science, 2000).

Fritz et al reference teaches eight cantilevers in a microfabricated silicon cantilever array (i.e. array of microsensors; membranes linear array; two-dimensional array), each cantilever functionalized on one side with a different oligonucleotide base sequence (i.e. functionalized), wherein hybridization of the base sequences with complementary oligonucleotide causes functionalized cantilever to bend (i.e. deflect when exposed to target molecules). See Figures 1-2 and captions. In addition, Fritz et al teach that the bending of each cantilever is measured using an optical beam deflection technique that detects reflected light (i.e. an optical beam source; an optical detector), wherein a linear VCSEL array provides a surface-emitting laser (i.e. collimated beam of laser light) to each cantilever (i.e. configured to simultaneously direct an optical beam onto each of the microsensors). See page 316, middle column, 2<sup>nd</sup> paragraph, lines 11-13; and page 318, right column, reference 14. Furthermore,

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Fritz et al teach that absolute deflections and simultaneous differential signals were recorded during hybridization (i.e. detector array simultaneously detect the position of each of the microsensors; detection in real time; detecting movement of beams of light reflected by each of the microsensors). See page 316, right column, 1<sup>st</sup> paragraph, lines 20-27.

With regards to claims 67-69, Fritz et al teach that the base sequences are immobilized on the gold-covered side (i.e. reflective paddle; stiffened portion) of the cantilevers. See page 316, middle column, 2<sup>nd</sup> paragraph, line 14 to right column, 1<sup>st</sup> paragraph, line 2.

With regards to claim 77, Fritz et al teach that one cantilever is functionalized with a 12-mer oligonucleotide and another with a 16-mer oligonucleotide (i.e. functionalized to detect different target molecules). See page 316, right column, 1<sup>st</sup> paragraph, lines 2-6.

With regards to claims 78 and 80, Fritz et al teach that hybridization experiments were performed in a liquid cell (i.e. at least one of the microsensors is positioned to be submerged in a fluid cell), wherein buffer solution is manually exchanged by a micropipette (i.e. flow of fluid sample can be stopped in the fluid cell). See page 316, middle column, 2<sup>nd</sup> paragraph, lines 8-11; and page 318, reference 13.

With regards to claim 79, since Fritz et al teach that hybridization is performed in a fluid cell and that optical detection is performed in real time, as stated above, it is necessarily required that the fluid cell be transparent to the optical beam in order to perform the hybridization assay and detection.

***Claim Rejections - 35 USC § 103***

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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16. Claim 74 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fritz et al. (Science, 2000) in view of Park et al (US 5,448,399).

Fritz et al reference has been disclosed above, but fails to teach that the optical detector array is a CCD array.

Park et al reference teaches a CCD camera that captures reflected light from a sample on a cantilever, in order to output an image of a probe or sample to a video display. See column 25, lines 31-40.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus of Fritz et al with a CCD camera that captures reflected light from a sample on a cantilever, as taught by Park et al, because the CCD camera provides an image of sample capture on the cantilever, which is more easily visualized than the graphical representations of Fritz et al. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including a CCD camera, as taught by Park et al, in the apparatus of Fritz et al, since Fritz et al teach optical detection on cantilevers, and the CCD camera of Park et al is also used to detect cantilevers.

17. Claim 75 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fritz et al. (Science, 2000) in view of Quate et al (US 6,203,983).

Fritz et al reference has been disclosed above, but fails to teach that the optical detector array is a CMOS array.

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Quate et al reference teaches a CMOS microelectric processing system, in order to easily integrate with silicon-based micromechanical devices such as cantilevers and to produce seamless sensors at low cost and integrate them directly into computers. See column 2, lines 11-23.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus of Fritz et al with a CMOS microelectric processing system, as taught by Quate et al, because the CMOS detectors are low cost, can be easily integrated into computers, and can be utilized with silicon-based cantilevers. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including a CMOS system, as taught by Quate et al, in the apparatus of Fritz et al, since Fritz et al teach silicon-based cantilevers, and the CMOS system of Quate et al can be integrated with silicon-based cantilevers.

18. Claims 76 and 81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fritz et al. (Science, 2000) in view of Lee et al (US 5,807,758).

Fritz et al reference has been disclosed above, but fails to teach that at least one microsensor is not functionalized to deflect when exposed to the target molecules.

Lee et al reference teaches a reference cantilever 82 (i.e. microsensor not functionalized) in proximity to a modified cantilever 12, in order to eliminate sources of noise, including non-specific binding. See column 8, lines 44-64; and Figure 8.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus of Fritz et al with a reference cantilever 82 (i.e.

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microsensor not functionalized) in proximity to a modified cantilever 12, as taught by Lee et al, in order to eliminate sources of noise, including non-specific binding, which allows clearer detection of sample binding on the cantilever of Fritz et al. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including a reference cantilever, as taught by Lee et al, in the apparatus of Fritz et al, since Fritz et al teach an array of cantilevers, and the reference cantilever of Lee et al is capable of being placed in an array of cantilevers.

With regards to claim 81, Lee et al teach that the cantilever can be detected by an interferometer. See column 8, lines 31-40.

### ***Conclusion***

19. No claims are allowed.

20. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure:

Sofield et al (US 2002/0072127 A1) teach a plurality of microcantilevers coated with different receptors and located in individual wells.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

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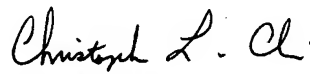
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Leon Y. Lum  
Patent Examiner  
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7/11/05